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Toxicity Criteria Used in Judging the Labeling of Pesticides

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Our Association long has pressed for protective legislation to guard the nation from dangerous substances, whether offered as foods or for use as pesticides. This paper explaining the general principles upon which the current program of federal control for the latter is based becomes of interest to all.

Throughout the history of this country, as soon as a new chemical was found to be outstandingly useful in controlling a pest, its wholehearted adoption was more a matter of distribution than of time. The fact that some of these materials possessed definite hazards to the users was recognized, but generally was accepted as an inescapable characteristic of an effective product. This is equally true of other chemical specialties, such as new drugs, detergents, polishes, solvents, or other household products, since for many years all that was needed to insure successful introduction of a new material was that it would give superior or more economical performance in controlling a pest, in treating a disease, or in simplifying a household chore.

Such a situation invited promotional sales campaigns wherein the actual values of the products were subordinated in the attempt to sell them through exaggerated claims, and public-spirited groups began to realize that more stringent controls over drugs and poisons were needed, particularly as to quality and the claims for performance. Many years of persistent propagandizing and aggressive action, often in the face of industrial opposition and public apathy, resulted in the passage of the Food and Drug Law in 1906 and the Insecticide Act in 1910. Most members of this Association are well acquainted with the former act, but may not be so familiar with the latter.

The Insecticide Act of 1910 served to insure the purchaser of an insecticide that he would receive an effective product which would contain the quantity of active ingredients claimed for it.

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For some 37 years this law was the principal federal statute dealing with the particular classes of pesticides for the control of which it was designed. Many years before its revision in 1947, however, the fact was recognized that certain classes of pesticides which were not included in the 1910 law also needed control, and that many other features of poison handling not related to performance and purity were highly important. So it was that the discovery and introduction of DDT, 2, 4-D, BHC, chlordane, TEPP, parathion, alphanaphthylthiourea, sodium fluoroacetate, and a host of other new and spectacular insect, weed, and rodent killers in the period from 1935 to 1945 presented problems for which there were no answers. For a short time after these new poisons appeared, the historic system of judging the acceptability of new pesticides exclusively on their performance remained in force and there was no federal law to prevent their widespread sale and general use.

Forward-thinking health, medical, and enforcement officials soon appreciated, however, that public safety in the new "chemical age" was going to demand more information about a poison than just its capacity for killing the pest. As a consequence, the work of revising the act of 1910 was pushed, and provisions were written into the new law permitting the Department of Agriculture to require on a pesticide precautionary labeling adequate, when complied with, to protect the public. It was given authority, also, to request toxicologic information on the new poisons sufficient to determine the adequacy of that labeling. All of this was made a part of the information needed to justify registration of the poison, and registration was made obligatory for every pesticide to be shipped in interstate commerce. Following proper public hearings on the bill, the Congress passed the measure and it was made into law on June 25, 1947, with effective dates on December 25, 1947, and June 25, 1948, as to the different pesticides to be covered.

The immediate effect of this new law was to bring to a halt the indiscriminate introduction of strange new poisons into interstate commerce. Almost immediately it became apparent that enforcement of the safety provisions of the Federal Insecticide, Fungicide, and Rodenticide Act was to be a most involved proposition. These provisions were intended in the first place to insure that the user of a poison be informed on the label, in clear and nontechnical language, as to just what dangers he faced in handling the material—and how to avoid injury to himself. Next, they were intended to point out to the user how the product must be employed to avoid hazards to the beneficial forms of life which might be covered by the spray itself or to the innocent bystander who might wander into a treated area before the poison had dissipated. And finally, they were intended to permit controls over permissible dosages and directions for use which would guarantee that the residues left on the food crops would be within acceptable limits.

Since these responsibilities were so all-inclusive, and since the agency in the Department of Agriculture to which the functioning of the law was assigned was a small organization, authority for cooperation with other governmental agencies was granted in the act. So it is that hazard problems of new poisons are discussed with the Public Health Service and food residue evaluations with the Food and Drug Administration. This procedure is operating quite smoothly and is much less complicated than it might appear to be.

To show the effects of the Federal Insecticide, Fungicide, and Rodenticide Act in reducing the hazards of using poisons, however, it is of interest to review briefly just how difficult it is for a research chemical to become a pesti-

cide. At the outset it is rarely possible for the chemist who synthesizes the new candidate product to forecast what specific pesticidal value it will have. That this is inevitable is shown by the fact that it might be useful as an insect killer, an insect repellent, a fungicide, a weed killer, a bactericide, a rodenticide, a rat or mouse repellent, a rabbit or porcupine repellent, or a disinfectant. Chemical structure does not necessarily give a hint as to where the value might appear. Early work on a chemical usually includes screening for effectiveness in the particular pesticidal field for which the laboratory making it was established. Then, when a use has been discovered, it is essential for the commercial agency that will exploit the chemical to undertake a minimum toxicologic evaluation. For every new pesticide that means determination of its acute oral toxicity and some information on its skin absorbability and inhalation hazard. These data are necessary to determine the types of danger the user may encounter in using the poison.

With this preliminary information at hand the need for further toxicologic study and the extent to which it must be carried is based on the type of use for which the chemical is intended. A material that will be used on the turf of a golf course once a year would require much less complete toxicologic examination than one used five or six times a year on a food crop or one used in household sprays where it could be employed every time a fly, gnat, or mosquito invaded the kitchen or nursery, or an ant or cockroach was found in the kitchen.

It is well to emphasize again at this point that the Federal Insecticide, Fungicide, and Rodenticide Act is a labeling law and not a prohibitory statute. Authority is not granted to exclude a poison from interstate sale, provided its labeling is adequate to protect the public. In this regard, the basic concept of the law is that an individual of ordinary intelligence is competent to read and follow label directions, and if those directions are adequate when complied with to prevent injury that is as far as this law is expected to go.

As was implied above, however, the amount of toxicologic information that may be needed to determine the adequacy of the precautionary labeling and the proper directions for use may be quite extensive. For example, the new chemical may have been found to have utility in controlling an insect on food crops and the preliminary toxicity data may have shown that it could be used with the normal precautions, since no unusual hazards to the user had been disclosed and the opinion of the Public Health Service on the precautionary labeling had been favorable. Use of the chemical on foods, however, could not be approved due to lack of long-term pharmacologic data and adequate chemical residue analysis. Without such information at hand, there was no basis for judging the adequacy of the directions or for requesting formal Food and Drug Administration concurrence in the proposed use. The complexity of this review is recognized by the fact that new poisons are accepted for specific uses as residue data on each crop become available, and the results of long-term feeding studies show that the residues found are within safety limits.

Many times two-year feeding tests on rats, one-year feeding tests on a nonrodent species, and complete pathology on these test animals are essential. Sensitive new chemical or biologic methods for residue analyses are needed and extensive residue data must be available before any use on a food crop can be registered. In this way poisons have been kept out of food use until the proposed application has met the requirements of both the Department of Agriculture and the Food and Drug Administration.

These discussions have applied largely to agricultural poisons which leaves household pesticides in a peculiar category of their own. Where a chemical has toxicologic characteristics that would require the use of protective clothing and masks or respirators to give adequate protection, it is possible to show that such a product is not suitable for household use other than by professional pest control specialists. Where the hazards are of a less spectacular, but more insidious nature, however, the problem is more involved.

It is essential to have reasonably complete acute oral toxicity, skin absorption, and inhalation data on a spray intended for use in the home. This information must be supplemented by skin irritation or sensitization studies if the product is to be proposed as a mothproofer, insect repellent, or for other uses where it will contact the skin, and by repeated inhalation tests if it is to be used in an aerosol or hand sprayer. When data which appear adequate to the Department of Agriculture have been submitted, the Public Health Service is asked to comment on the proposed labeling and on the propriety of the suggested uses. Following this, registration may be considered.

It is apparent from this summary that there are no simple, fixed procedures which may be followed by a manufacturer and, when results are favorable, will always insure acceptance of a pesticide for interstate sale. The attitudes of physicians and pharmacologists toward chemicals vary as new laboratory findings or experiences in use become available and legal requirements should not be so precise that new concepts of hazard or safety cannot have prompt consideration.

Shifting of scientific opinions is an added problem for the law enforcement official, however, since he must attempt to determine the legal significance of any new philosophy toward the product. Too often the impression he gets upon investigation is that there is a wide difference of opinion among experts and many times he finds that the same data are given widely divergent interpretations by equally qualified laboratories.

Under those conditions it has been maintained by the administration of the Federal Insecticide, Fungicide, and Rodenticide Act that public interest is served to best advantage by maintaining a flexible procedure whereby each poison may be studied individually and on its own merits. It is felt that when data on a poison requested of a manufacturer by the Department of Agriculture is acceptable to its specialists, as well as those of the Public Health Service or the Food and Drug Administration, the proposed use should be registerable.

There is no doubt but that the Federal Insecticide, Fungicide, and Rodenticide Act has had a major effect on the speed of introduction of new poisons, and certainly it is no longer true that a pesticide can be placed on the market without pretesting, as was charged more legitimately before 1947. In addition, there is a provision in the law that permits cancelation of a full registration on the motion of the Secretary of Agriculture. This action must be followed immediately, however, by the issuance of a registration under protest which is to be accomplished by a letter to the manufacturer explaining in detail why the action to cancel was taken. Such a procedure permits prompt action to notify a manufacturer that unfavorable use experience has indicated need for curtailing distribution of his product.

The latest legislative move made in this field of pesticide control deals entirely with the establishment of safety limits for economic poisons on raw agricultural commodities. This bill was the outgrowth of extensive hearings held in 1950, 1951, and 1952 before a Select Committee of the House of Representatives to investigate the use of chemicals

on food products. It took the form of an amendment to the Food, Drug, and Cosmetic Act and following the usual hearings and revisions was made law on July 22, 1954.

The wording of the amendment gives industry the responsibility for assembling performance, residue, and toxicologic data upon which may be judged the safety of the proposed tolerance for the product in foods. It makes the Department of Agriculture responsible for reviewing the performance and residue data submitted and then for certifying to the Food and Drug Administration as to the usefulness of the product and as to the reasonableness of the proposed tolerances in the light of the residues found when the poison was used as required to give control of the pest involved. It is then the responsibility of the Food and Drug Administration to determine the safety of the proposed tolerance. Such a procedure takes advantage of the experience and facilities of both agencies of government and it is felt that this will serve the public interest most effectively. It is contemplated that a new chemical will not usually be registered for application to food until its safety has been established by this procedure and a tolerance which can be met by using the product in accordance with sound directions has been set.

It would be unrealistic to imply that there are no problems left in the legal controls over new economic poisons. And it must be admitted that just as serious problems remain, also, regarding further controls over useful drugs, firearms, cars, planes, and other useful things which serve—and endanger—us daily in this modern world. It is encouraging, however, to be able to report to the American Public Health Association that much progress in pesticide management has been made in the few years since 1947.

The future of poisons control cannot be forecast with certainty, but already it is apparent that the public is demanding increasing protection against insidious chemical agents, whether they be smog, car gas, industrial fumes, strong drugs, household chemicals, intentional food additives, or pesticides.

An informed American Public Health Association will do much to make new moves realistic so that the dangers inherent in chemical use may be guarded against, while the values of such use can be preserved for the never-ending fight against economic loss, discomfort, and disease.

Among the recommendations made by the Task Force on Medical Services to the Commission on Organization of the Executive Branch of the Government, is the following:

"That the Department of Health, Education, and Welfare provide more leadership and assume more responsibility in planning and carrying out the programs of the federal government that relate to civilian health, exploring sound means within public policy of assisting the American people to improve their own health."

(From the Report on Federal Medical Services. Prepared for the Commission On Organization of the Executive Branch of the Government by the Task Force on Medical Services, February, 1955.)